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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/010,050	11/09/2001	Paul O. Sheppard	97-38C1	7831

7590 06/16/2004

EXAMINER
MITRA, RITA

ART UNIT	PAPER NUMBER
1653	

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DATE MAILED: 06/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/010,050	PAUL SHEPPARD	
	Examiner	Art Unit	
	Rita Mitra	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/19/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

It should be noted that due to an oversight Applicants' preliminary amendment was not considered and a restriction was made to original claims 1-34 in office action dated February 25, 2004. In response Applicants elected Group II, claims 12-19 and 23-32 without traverse filed on April 1, 2004.

Restriction requirement in office action of February 25, 2004 is withdrawn in view of Applicants' preliminary amendment filed on March 30, 2004. Claims 1-33 have been canceled. New claims 34-51 have been added and entered. Therefore, claims 34-51 are currently pending and are under examination.

Information Disclosure Statement

The information disclosure statement filed on March 19, 2002 is acknowledged. Applicants have indicated that they have not included copies of the documents listed on the 1449 form that were previously cited by or submitted to the patent office in a prior application 09/122383. However, copies of the references listed in PTO Form 1449 are missing from the prior application. Please note that the references A1 to A88 on 1449 have been lined through. Consideration of the lined through references will be made upon compliance with 37CFR 1.98 (a) (2).

Claim Rejections - 35 USC § 101 (Non-statutory)

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 40 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim recites a "cultured cell" which reads on the natural, non-patentable, state of the cultured cell. The rejection would be obviated

by the insertion of language indicating that the cell was isolated, thus being removed from the natural environment.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title"

Claims 34-51 are rejected under 35 U.S.C. 101 because the specification does not provide either a specific or substantial asserted utility or a well-established utility, and thus, does not support the claimed invention. The DNA segment in the claimed expression vector encoding the polypeptides are not supported by either a substantial asserted utility or a well established utility because the specification fails to assert any utility for the claimed DNA encoding the polypeptides and neither the specification as filed nor any art of record disclose or suggest any activity for the claimed DNA encoding the polypeptide such that another non-asserted utility would be well established. Note, because the claimed invention is not supported by a substantial asserted utility for the reasons set forth above, credibility cannot be assessed.

The specification, on pages 14-16, describes a DNA that encodes a secreted Zsig46 polypeptide, wherein the DNA sequence is found on human chromosome 13. Applicants assert (page 14) that based on potential N-glycosylation sites and post-translational processing sites located on SEQ ID NO: 2 the polypeptides may be released as an active polypeptide. But, no biological activity has been set forth in the specification as filed for the Zsig46 polynucleotide (SEQ ID NO: 1) and encoded polypeptide (SEQ ID NO: 2) and fragments thereof (page 16), other than that it "may be used in the study of secretion of proteins from cells." However, speculative biological activities have been provided on pages 25, 34 of the specification. For example, the use of the polypeptides for identification and isolation of receptors involved in Zsig46 binding and signaling process is described here (page 34). The art does not disclose anything regarding the

significance of said receptors. Therefore, this utility is not well established and substantial.

Similarly, assertion of use of the claimed highly conserved amino acids within a protein family as a tool to identify new family members (page 24). The specification does not indicate what would be the function of those new family members. There is not disclosed or "real world" utility associated with the polypeptides encoded by the claimed DNA. Thus, the utility is not substantial.

Applicants assert on page 25 of the specification that the pharmaceutical composition comprising purified Zsig46 would be useful in the prevention or treatment of conditions associated with chromosome 13q. Examples of many diseases have been listed but the specification does not indicate any correlation of the role of a Zsig46 composition to a specific disease treatment or prevention. Also, high expression of Zsig46 in thyroid tissue does not lead one to conclude that Zsig46 polypeptide would be useful in treatment or prevention of thyroid diseases.

Other activities that the DNA or polypeptides encoded therein may exhibit are listed throughout pages 25-36, 54, 61-66 of the specification. However, these activities are purely speculative because the claimed invention is not supported by a substantial asserted utility for the reasons set forth above. In summary, the DNA encoding the polypeptides claimed do not have a substantial or well-established utility and therefore lacks utility under 35 U.S.C. 101.

Claims 34-36 are drawn to an expression vector comprising a DNA segment encoding a polypeptide comprising a fragment of SEQ ID 2, consisting of residues 31-346 (claim 34), residues 1-346 (claim 35), wherein the DNA segment comprises nucleotides 137-1084 of SEQ ID NO: 1 (claim 36). The specification does not describe the functional properties of these fragments, and the structural information is limited. While the specification enumerates several known assays for biological activity (p. 55-57), the specification does not guide the selection of a specific assay that would be used to screen the biological activities nor define what those biological activities would have been for the claimed fragments.

Claims 38 and 39 are drawn to an expression vector comprising a DNA segment, wherein the DNA segment further encodes a secretory signal sequence operably linked to the polypeptide (claim 38), wherein the secretory signal sequence comprises residues 1-28 or 1-30 of SEQ ID NO: 2 (claim 39). The specification indicates at page 45 that these novel secretory signal sequence fusion constructs can direct the secretion of an active component of a normally non-secreted protein, such as a receptor. However, the specification does not describe a specific fusion construct using signal sequence of SEQ ID NO: 2 that may be used to direct a specific peptide through the secretory pathway.

Claims 46-49 are drawn to an isolated polynucleotide encoding a polypeptide, wherein the encoded polypeptide comprises amino acid residues 31-346 of SEQ ID NO: 2 (claim 46), residues 1-346 of SEQ ID NO: 2 (claim 47), wherein the polynucleotide of claim 46 is DNA (claim 48) and comprises nucleotides 137-1084 of SEQ ID NO: 1 (claim 49). The specification does not describe the functional properties of these fragments, and the structural information is limited. While the specification enumerates several known assays for biological activity (p. 55-57), it does not guide the selection of a specific assay that would be used to screen the biological activities of the claimed fragments.

Claim 51 is drawn to an isolated polynucleotide encoding a fusion protein comprising two portions joined by a peptide bond, wherein the first portion is a polypeptide comprising amino acid residues 31-346 of SEQ ID NO: 2 and wherein the second portion comprises another polypeptide. It is not clear from the description of the Zsig46 fusion proteins (specification page 23) about the protein structure, aside from its first polypeptide amino acid sequence, and/or its function.

In the instant case, the failure of applicants to specifically identify why the claimed invention is believed to be useful renders the claimed invention deficient under 35 USC 101. No specific biological activity has been identified for the polynucleotide set forth in SEQ ID NO: 1, encoding a protein set forth in SEQ ID NO: 2 other than the fact that the protein may be secreted (p. 14-16). The person having ordinary skill in the art would not be able to identify any specific activity for the protein comprising or related to SEQ ID NO: 2 based on its structure alone for the reasons set forth above. General

statements that a composition has an unspecified biological activity or that do not explain why a composition with that activity is believed to be useful fails to set forth a "specific utility." Brenner v. Manson, 383 US 519, 148 USPQ 689 (Sup. Ct.1966) (general assertion of similarities to known compounds known to be useful without sufficient corresponding explanation why claimed compounds are believed to be similarly useful is insufficient under 35 USC 101).

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 34-51 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

The specification is objected to because the biological material used in the claimed process is a microorganism clone, which has been deposited with American Type Culture Association (ATCC) and has the accession number ATCC 98668 (plasmid pZp9, Example 4, pages 70-72). Since the clone is essential to the practice of the claimed invention it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. If the organism is not so obtainable or available, the requirement of 35 U.S.C. 112 may be satisfied by a deposit of the microorganism.

That the applicants have apparently incorporated specific references into the specification does not eliminate the issue of public availability and permanence as the vectors cited in the references and the references per se do not indicate, public availability of the starting materials in as much as the biological materials mentioned in a publication may be proprietary and not publicly available.

It is apparent that the claimed clone is essential to the claimed invention and the deposit is necessary for an adequate written description and enablement for the claimed invention. The specification needs a specific description or demonstration of reproducibility of the claimed DNA and encoded protein from the deposit. The reproducibility has not been demonstrated because no attempt was made to give a comparison of the positive clones generated in Example 5.

The specification on pages 71 and 72, indicates that clones containing the plasmid pZp9 was deposited, with the ATCC. Applicants should provide the current full address of ATCC as to read :

American Type Culture Collection (ATCC)

Patent Depository

10801 University Boulevard

Manassas, VA 20110-2209

If the deposit was made under the terms of Budapest Treaty on the international recognition of the deposit of microorganisms for purposes of patent procedure, Applicants should state this in the specification and also required to provide a photocopy of the receipt for the certificate of deposit. It is apparent that the claimed deposit material is essential to the claimed invention and the deposit is necessary for an adequate written description and enablement for the claimed invention. The Office notes that during the pendency of this application, access to the invention will be afforded to the Commissioner upon request where all restrictions upon availability to the public will be irrevocably removed upon granting of the patent and that the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer where the deposit will be replaced if it should ever become inviable.

Claims 34-51 are rejected under 35 U.S.C. 112, first paragraph, for the reasons set forth in the objection to the specification.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

"The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention."

Claims 35, 37, 39, 41, 44 and 51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 35 recites the limitation "residues 1-346 of SEQ ID NO: 2" in line 2. There is insufficient antecedent basis for this limitation in the claim. This renders the claim improper dependent claim and enlarges scope of claim 34.

Claim 37 is rejected because it is not clear how the DNA encodes affinity tag linkage.

Claim 39 recites the limitation "residues 1-28 or 1-30 of SEQ ID NO: 2" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claims 41 and 44 are rejected for using E. coli. The term "E. coli" should be preceded by the full spelled out word "Escherichia.coli."

Claim 51 is indefinite because of using the term "another." It is unclear what polypeptide is there in the second portion of the fusion protein, what is the structure and function of the second portion polypeptide?

Claim 51 is also rejected for the use of the term "portion." It is not clear how a fusion protein comprises a "portion."A correction to read "segment would obviate the rejection.

Conclusion

No claim is allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rita Mitra whose telephone number is (571) 272-0954.

The Examiner can normally be reached from 9:30 a.m. to 6:30 p.m. on weekdays. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Christopher Low, can be reached at (571) 272-0951. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (703) 872-9306. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0547.

R Mitra

Rita Mitra, Ph.D.

June 8, 2004

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